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Figure 1: Sedation Model

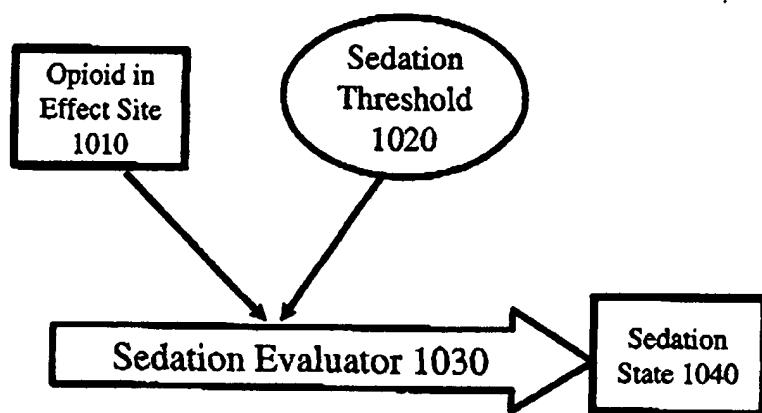


Figure 2: Ventilatory Depression Model

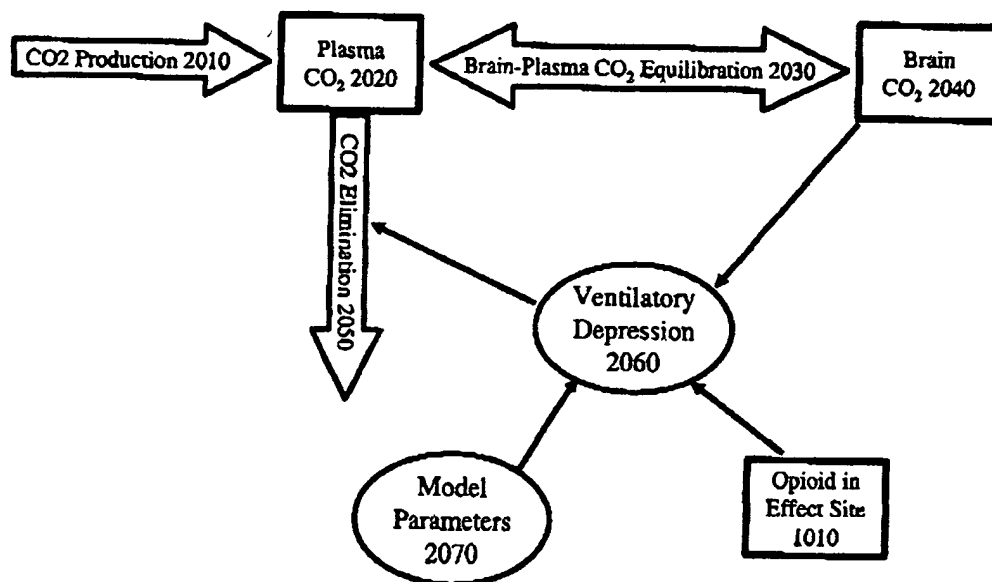
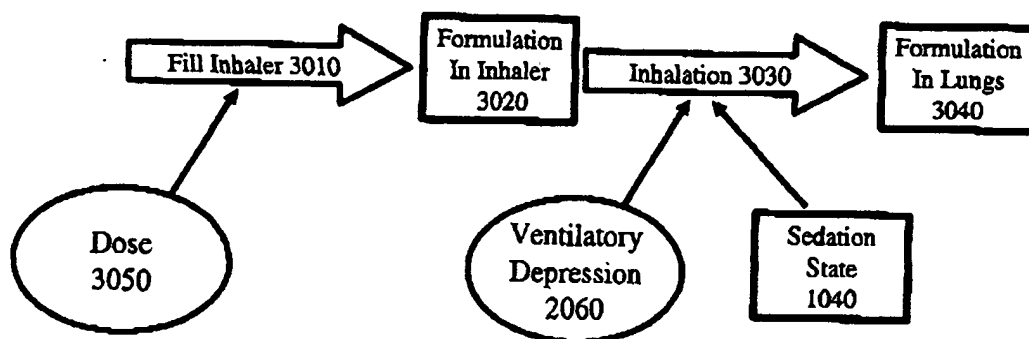


Figure 3: Device Model



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Figure 4: Pharmacokinetic Model

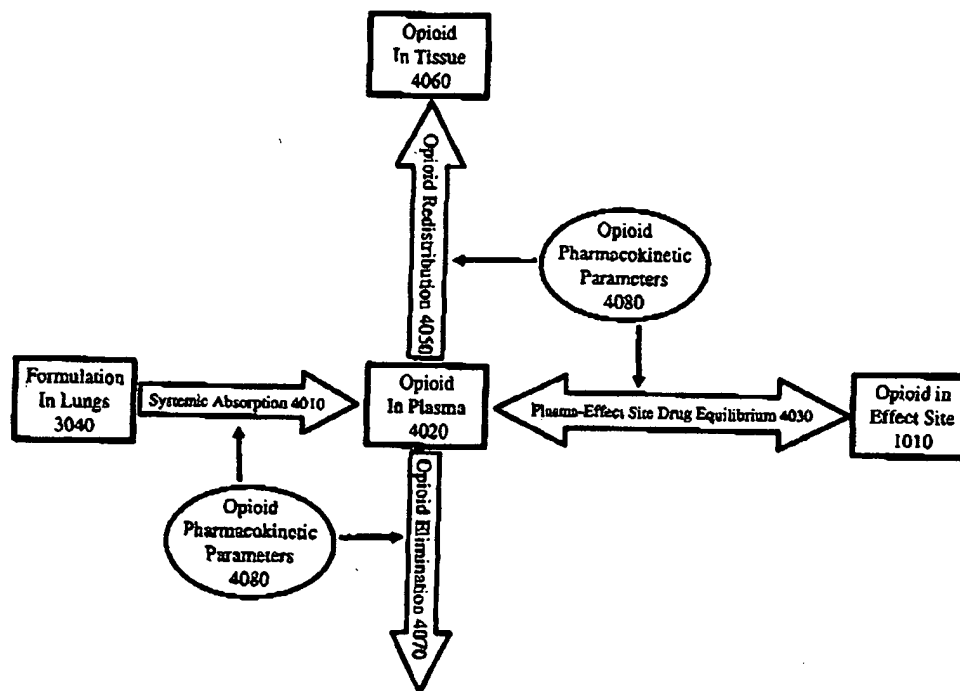


Figure 5

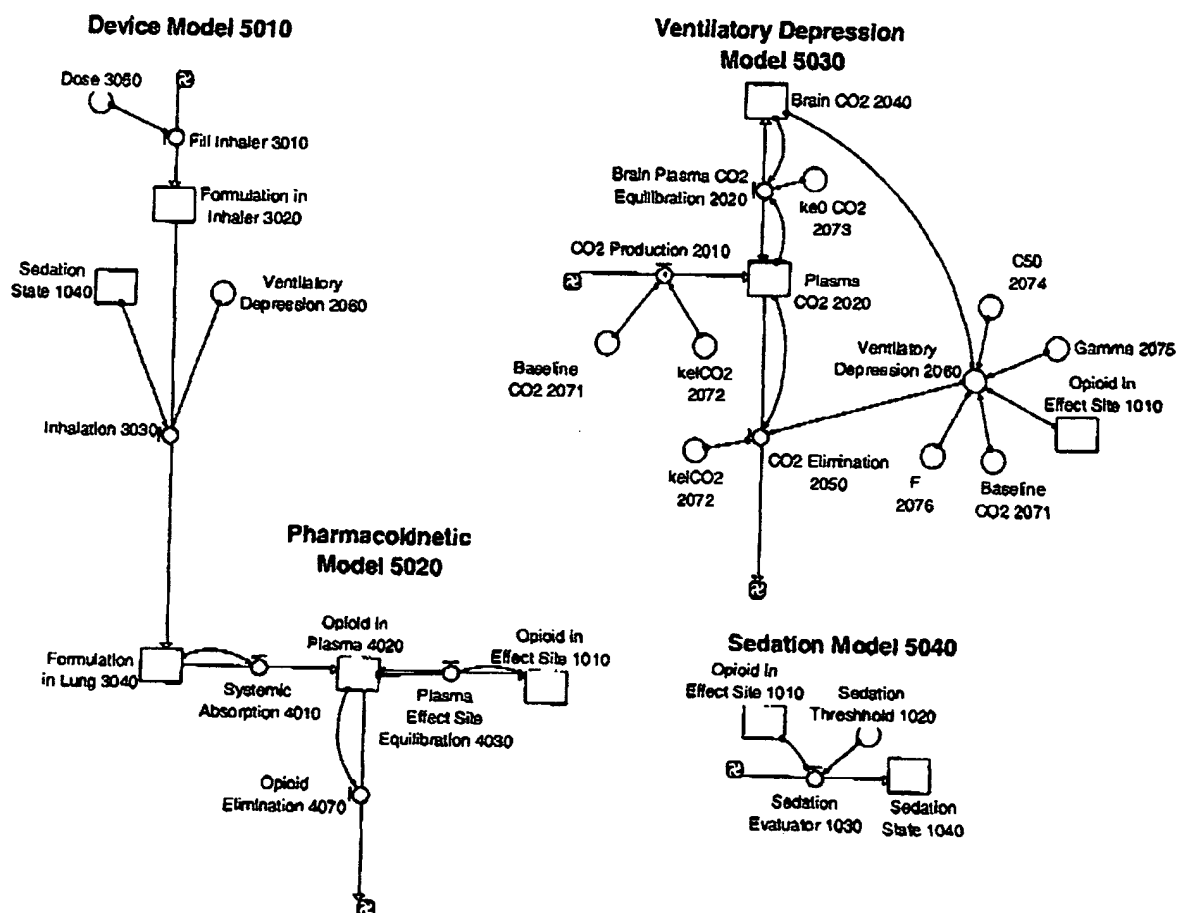


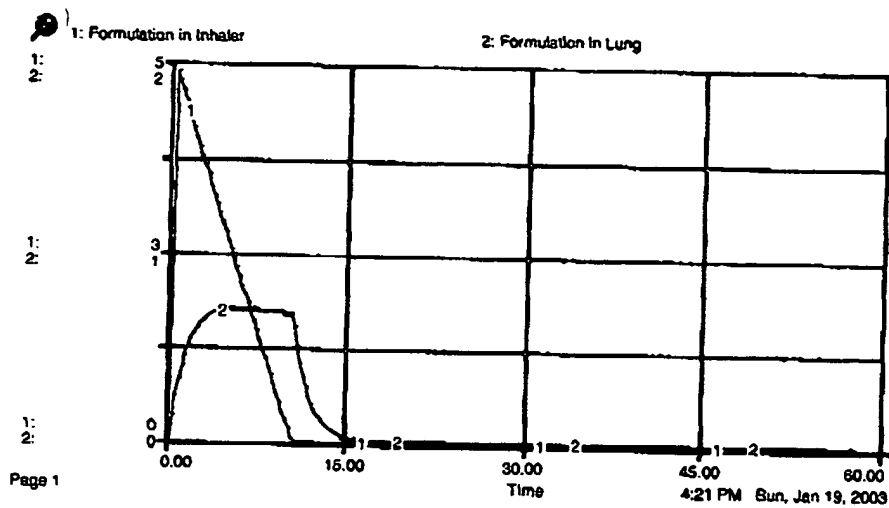
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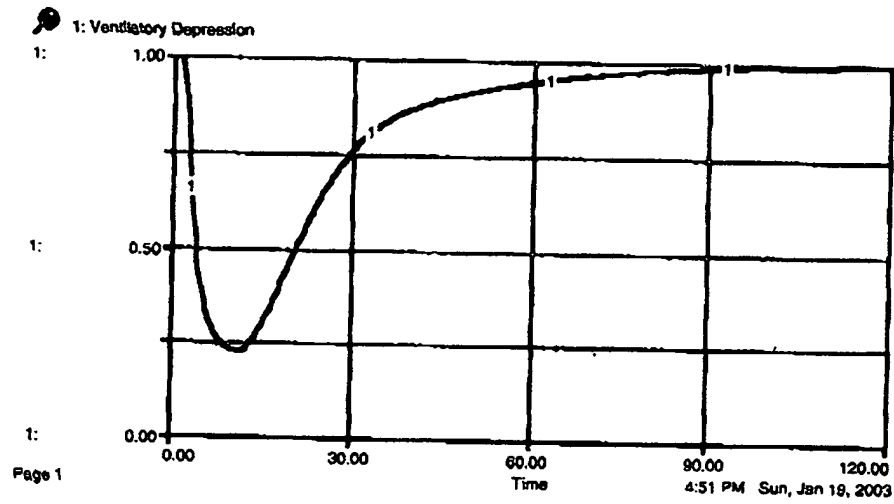
Figure 7**7/22**

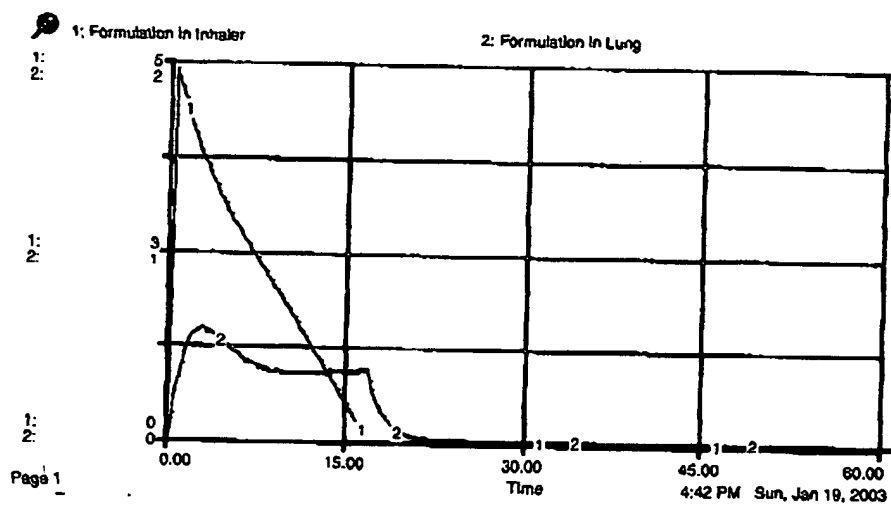
Figure 8**8/22**

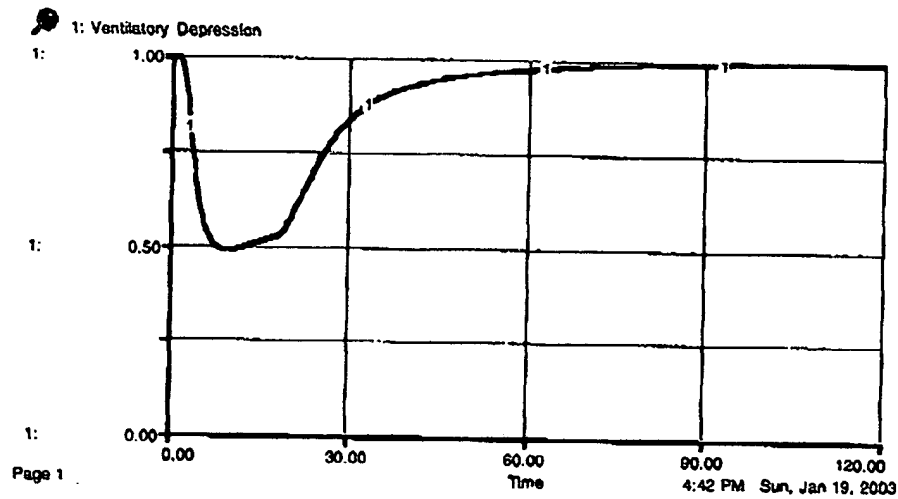
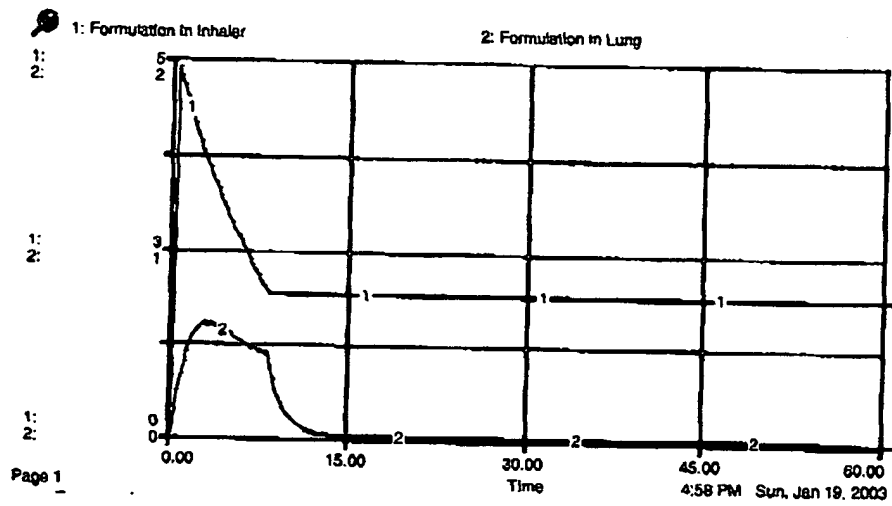
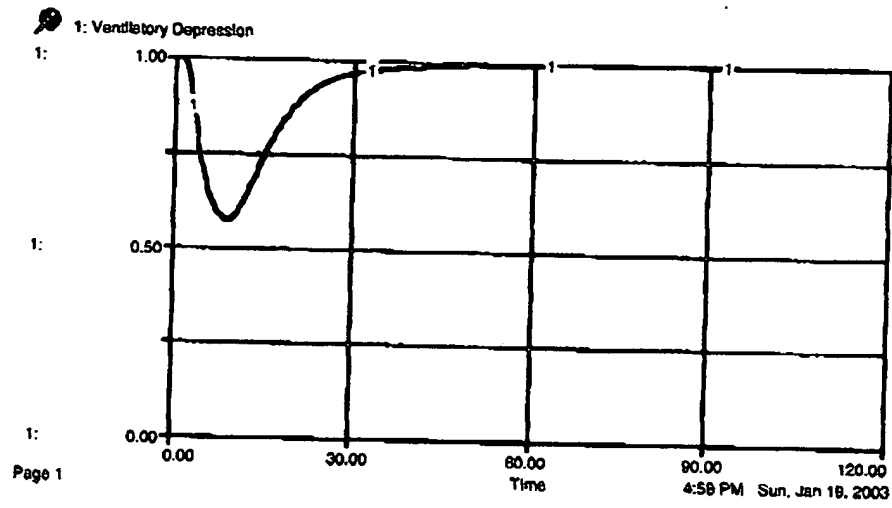
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Figure 11

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Figure 12: Two Opioid Model

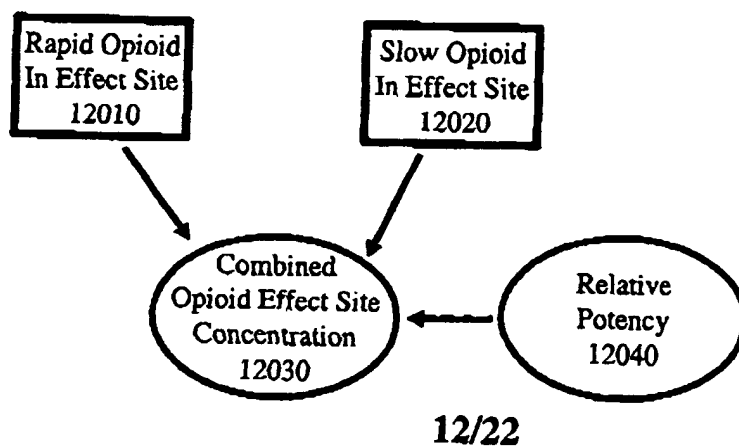


Figure 13: The elements of the invention, wherein two opioids are administered through inhalation.

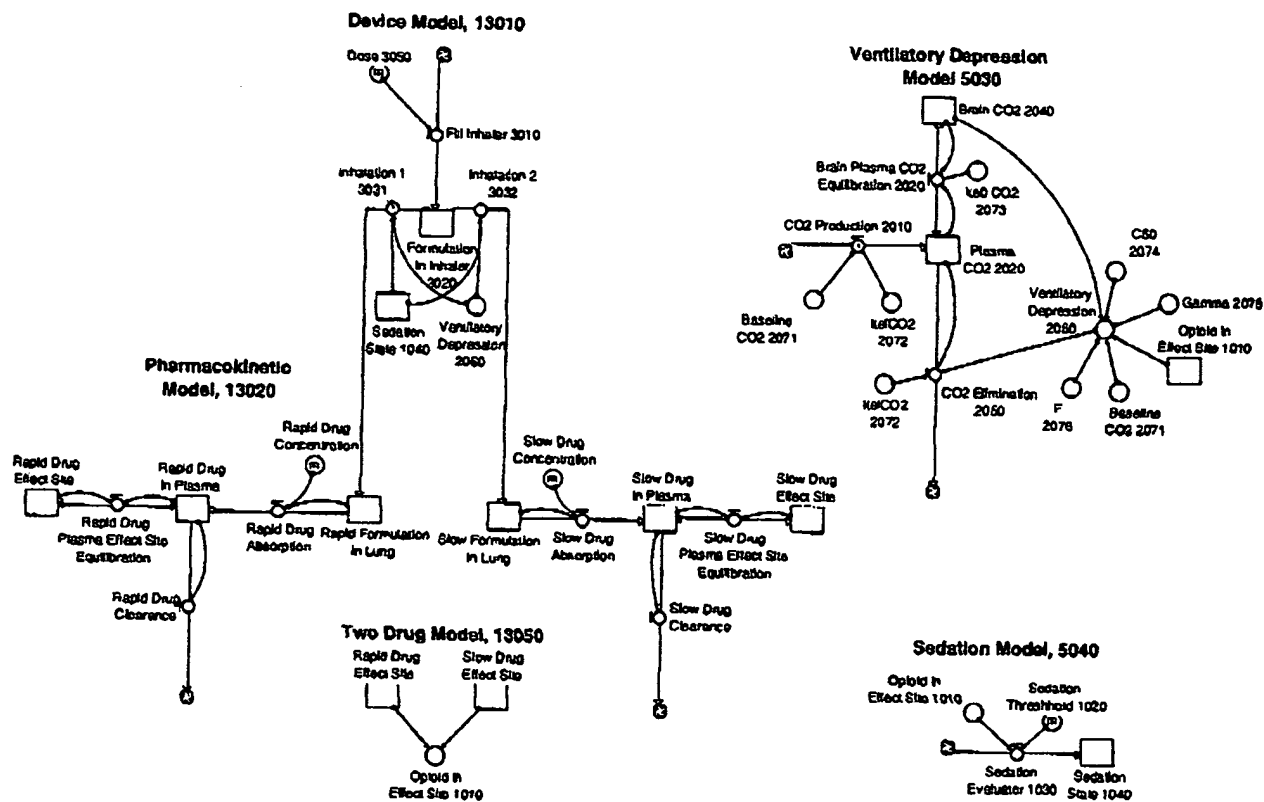


Figure 14: Drug in inhaler and lung in the presence of opioid-induced ventilatory depression and sedation for the two opioid model.

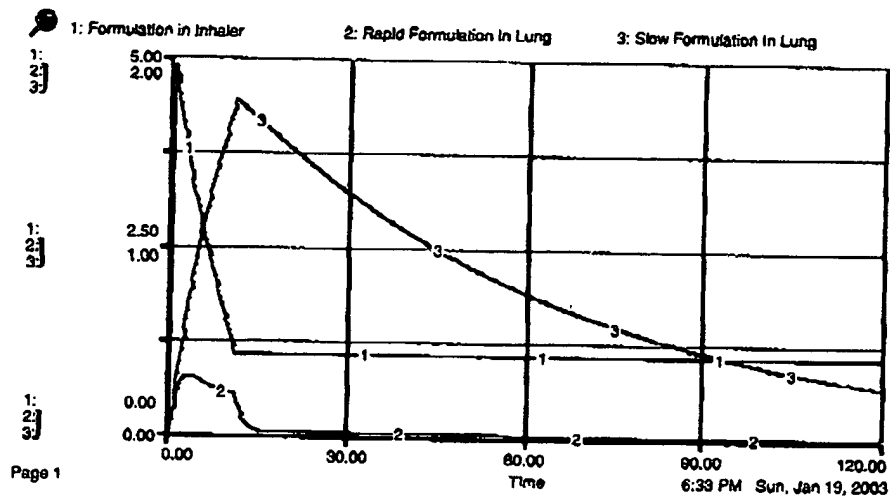


Figure 15: The rapidly acting opioid concentration in the effect site, the slowly acting opioid concentration in the effect site, and the combined concentration of opioid at the effect site, during two opioid administration with the device.

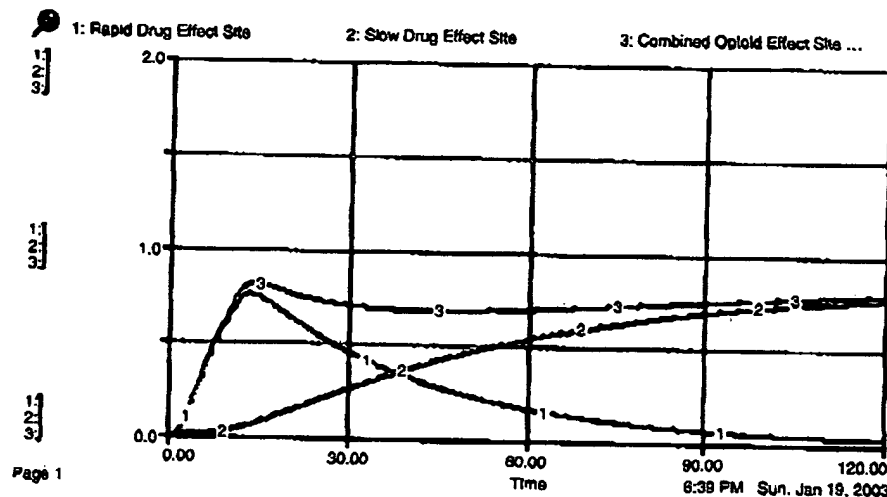


Figure 16: Ventilatory depression in the presence of self-limitation of opioid delivery from ventilatory depression and sedation with the two-opioid delivery system.

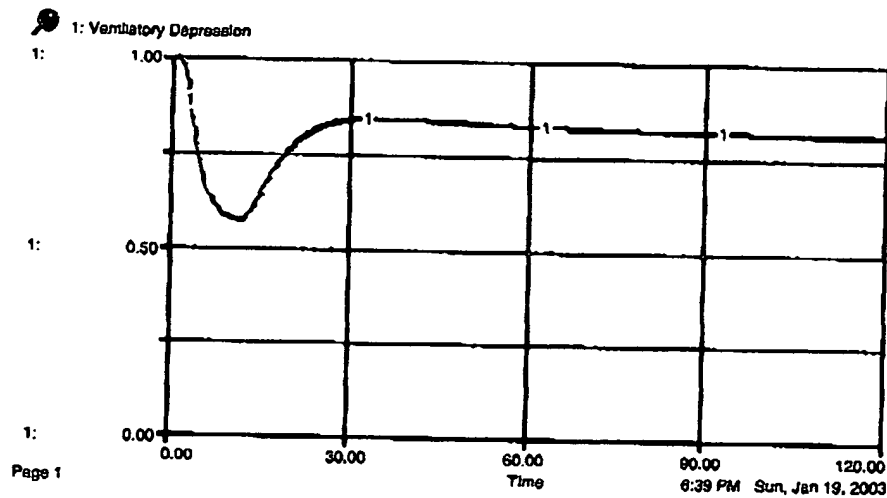


Figure 17: The elements of the invention, wherein two opioids are administered through inhalation, and the rapidly acting opioid is alfentanil, and the slowly acting opioid is morphine.

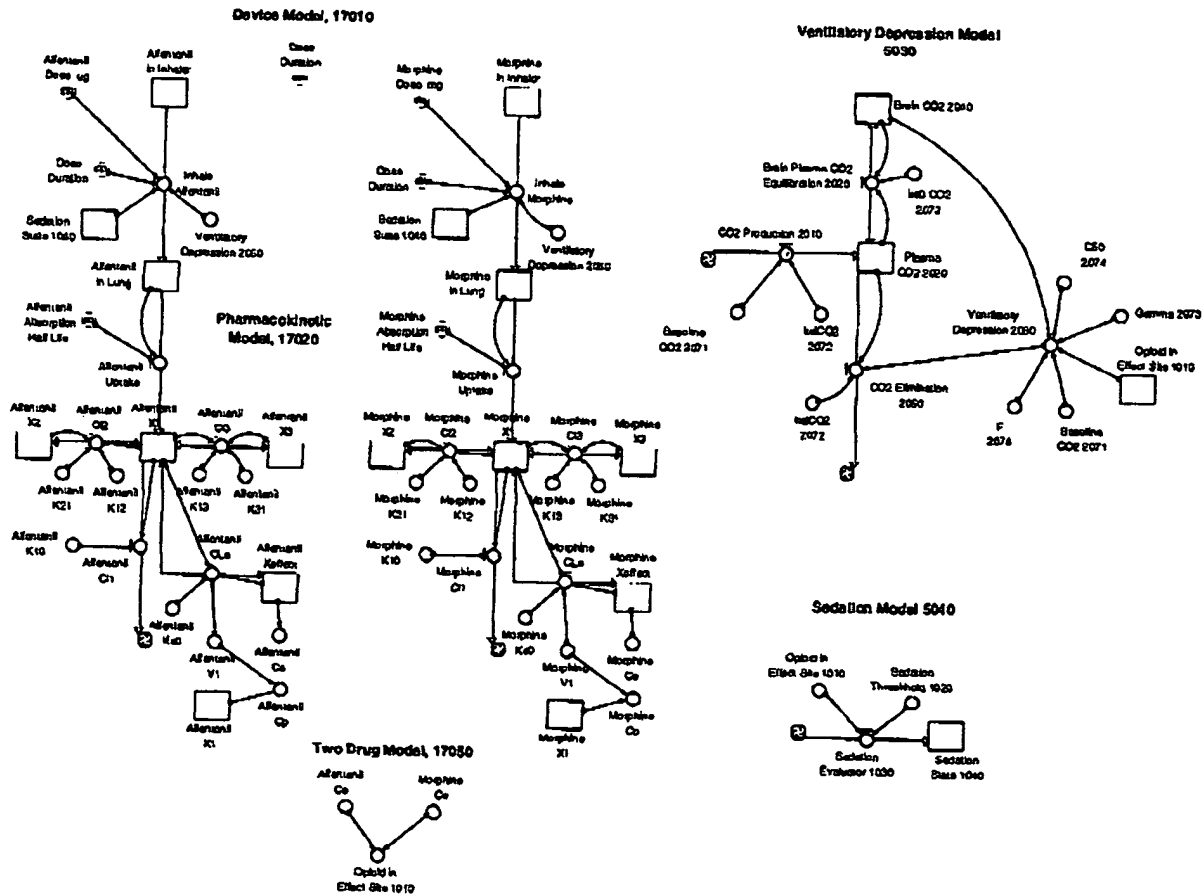
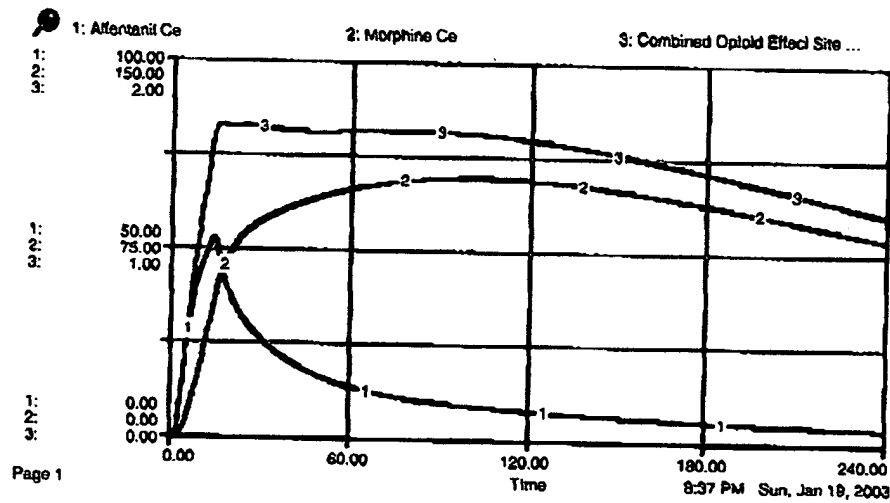
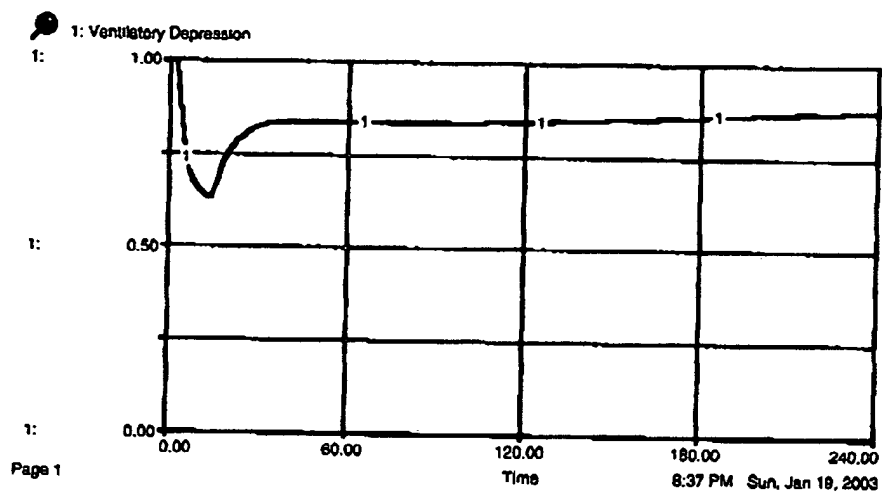


Figure 18: Alfentanil, morphine, and combined opioid effect site concentrations.



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Figure 19**19/22**

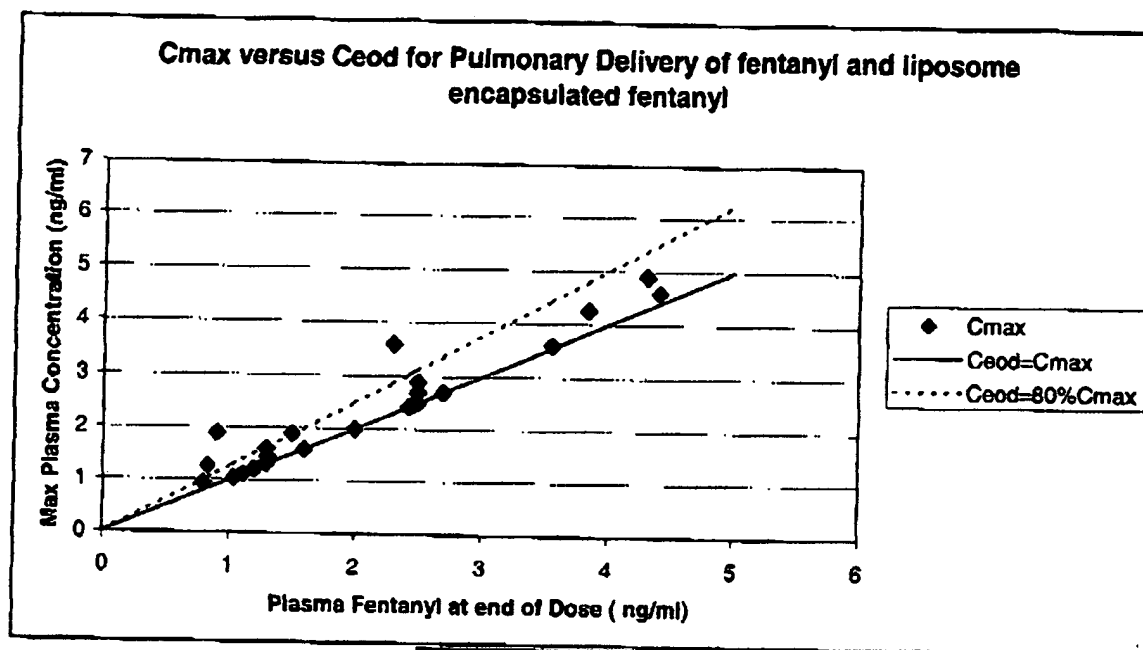


Figure 20A

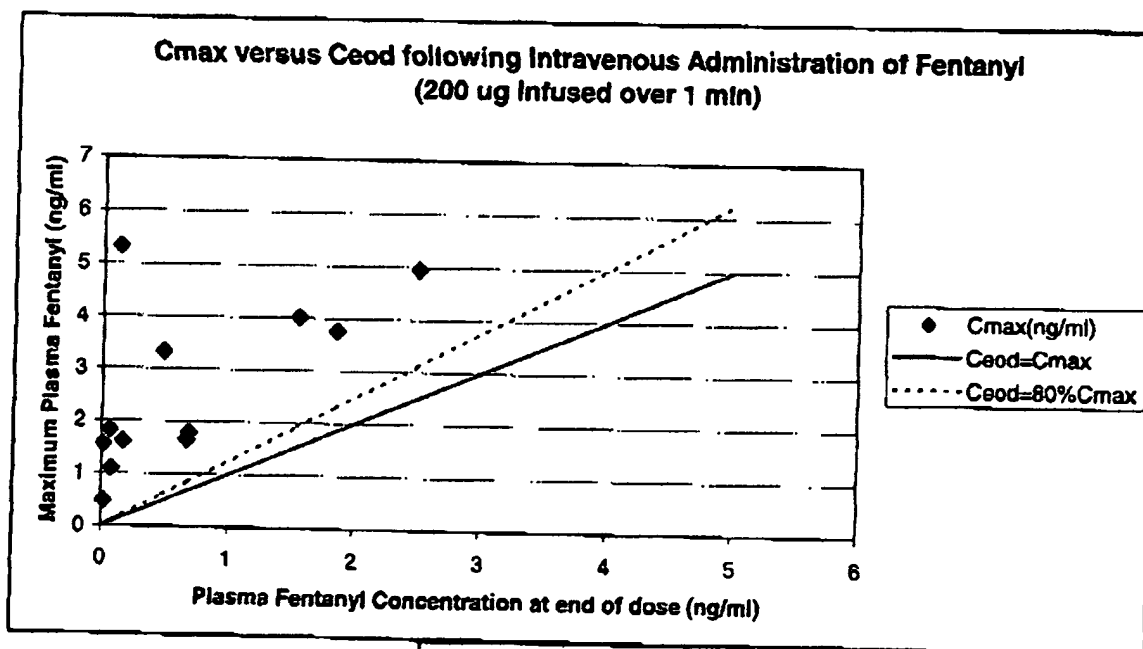


Figure 20B

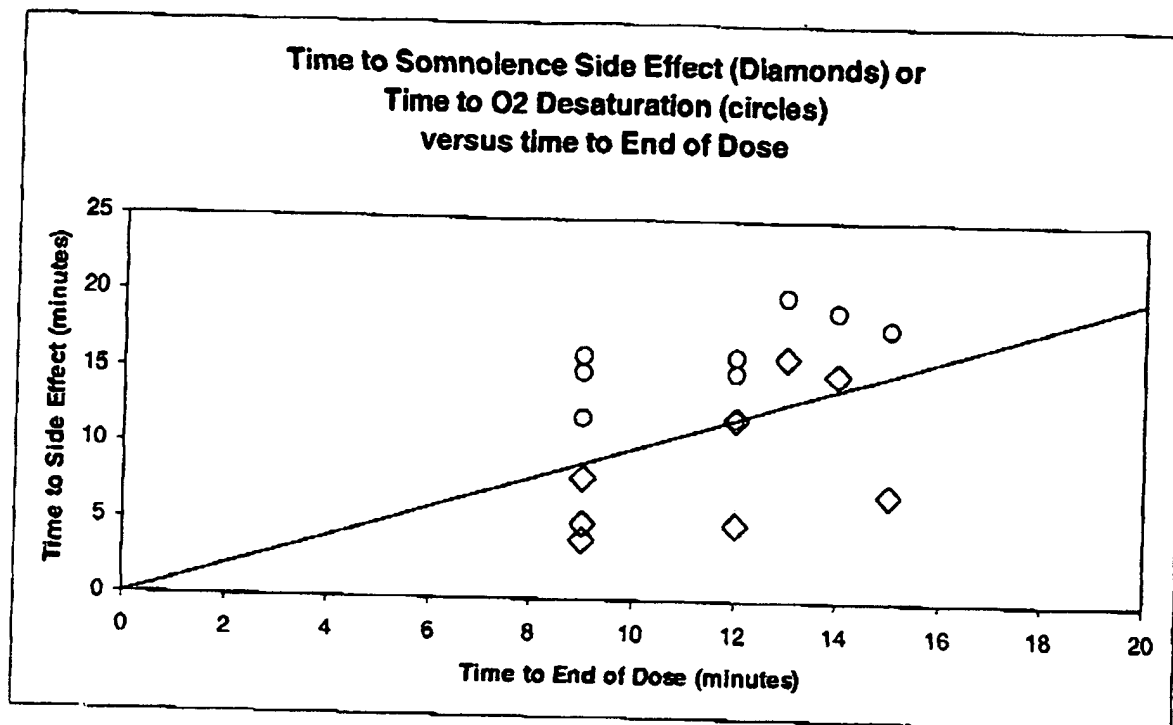


Figure 21

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| | No side effect | Side effect | |
|-------------|----------------|-------------|----|
| N | 26 | 24 | |
| No hypoxia | 22 | 14 | 36 |
| Hypoxia | 4 | 10 | 14 |
| Null effect | | | |
| No hypoxia | 18.72 | 17.28 | 36 |
| Hypoxia | 7.28 | 6.72 | 14 |
| P value | 0.038653124 | | |

Figure 22 – Correlation of side
effect to toxic event

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